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EDITORIAL · REDAKSIONEEL

DO GAY CITY DOGS (*GENUS* CANIS) SMOKE TOO MUCH?

Elsewhere in this issue we publish the proceedings of an international conference on the *Medical Aspects of Air Pollution,* held in Vienna last year. South Africa was represented in the list of participants who were drawn from all over the world.

The concern of the Conference with the serious medical consequences of air pollution is a timely reminder of the need not only to take stock of the hazards of industrialization but also to develop adequate prophylactic measures to prevent or reduce the incidence of serious disease.

Animal Studies: The Role of Comparative Pathology

A valuable and enlightening contribution to the discussions was the information to be derived from comparative studies on animals in cities as contrasted with those in rural areas. Farber emphasized our failure to make sufficient use of this valuable source of information. It appears from his remarks that there has been an increase of cancer in dogs living in cities as compared with dogs living in rural

ROOK VROLIKE STADSHONDE (*GENUS* CANIS) TE VEEL?

Elders in hierdie uitgawe publiseer ons 'n verslag oor die verrigtinge op die internasionale konferensie oor die Mediese Aspekte van Lugbesoedeling wat verlede jaar in Weenen plaasgevind het. Suid-Afrika was verteenwoordig in die lys van deelnemers wat uit alle dele van die wêreld gekom het.

Die belangstelling wat die konferensiegangers in die ernstige mediese gevolge van lugbesoedeling getoon het, is 'n tydige herinnering aan die noodsaaklikheid nie alleen om 'n inventaris van die gevare van industrialisasie op te maak nie, maar ook om doeltreffende profilaktiese stappe te doen om die verskyning van ernstige kwale te voorkom of te verminder.

Studies met Diere: Die Rol van Vergelykende Patologie

'n Waardevolle en insiggewende bydrae tot die besprekings was die inligting wat gegrond was op vergelykende studies met diere in stede in teëstelling met diere op die platteland. Farber het beklemtoon dat ons nie voldoende gebruik van hierdie waardevolle bron van inligting maak nie. Uit sy opmerkings blyk

areas. In cats there has been an increase in cancer of the tonsils, the oesophagus and the stomach. Chauncey Leake, reporting the views of Russian scientists, notes that they have also observed an increase of cancer in animals living in cities. This phenomenon has been reported in Holland and in England as well.

The evidence from veterinary pathology merely demonstrates once again the need to exercise the greatest scepticism in accepting glib inferences about aetiology when they depend upon purely statistical studies. The protagonists of cigarette smoking as a cause of lung cancer have steadily been forced to shift their ground and to recognize the importance (if not the overshadowing importance) of air pollutants other than those due to cigarette smoke.

Liebow,[1] in a review of bronchiolo-alveolar carcinoma, recently concluded that this type of lung tumour accounts for from 0.5 to 5% of all lung carcinoma. Several aetiological factors were considered, 'but no common factor has emerged.' Viruses have not been incriminated and, as similar tumours have been reported in dogs and sheep, it is not surprising that no attempt has been made to postulate cigarette smoking as a cause of the cancer.

HUMAN LUNG CANCER IN NEW ZEALAND, SOUTH AFRICA AND THE U.S.A.

Another interesting feature which emerged in the Vienna discussions was confirmation from Ohio of the work reported by Eastcott in New Zealand and Dean in South Africa. The Ohio studies covered immigrants from England, Wales and Italy who settled in Cuyahoga County, a very industrialized area. The lung cancer rates among the immigrants were much higher than among the native-born citizens; yet they were much less than in the immigrants' country of origin. Haenszel (of the National Cancer Institute) tested the Ohio findings in a national study of foreign-born immigrants in the U.S.A. His analysis, based on a study of immigrants from 12 countries, showed that these immigrants had a higher lung cancer rate than the native-born citizens of the United States. This confirms on a national scale the work reported from Ohio, New Zealand and South Africa.

1. *Advances in Internal Medicine, Vol. X.* Ed. by William Dock and I. Snapper. 1960. p. 343. Chicago: Year Book Publishers Inc.

dit dat, in vergelyking met honde op die platteland, kanker by honde in die stede toegeneem het. In die geval van katte was daar 'n toename in kanker van die mangels, die slukderm en die maag. Chauncey Leake wat verslag oor die sienswyses van Russiese wetenskaplikes gedoen het, het gesê dat hulle ook 'n toename in die aantal kankergevalle by stedelike diere waargeneem het. Hierdie verskynsel word ook uit Holland en Engeland gerapporteer.

Die bewyse wat deur veeartsenykundige patologie verstrek word, toon weereens hoe noodsaaklik dit is om groot skeptisisme aan die dag te lê voordat 'n mens oppervlakkige etiologiese gevolgtrekkings aanvaar, veral as sulke gevolgtrekkings op suiwer statistiese studies berus. Die voorstanders van die teorie dat die rook van sigarette 'n oorsaak van longkanker is, is in die jongste tyd herhaaldelik gedwing om van stelling te verander, en om die belangrikheid (en miskien die oorwegende belangrikheid) van lugbesoedelingsmiddels, behalwe dié wat van sigaretrook afkomstig is, te erken.

In 'n oorsig van brongiolo-alveolêre karsinoom het Liebow[1] onlangs tot die gevolgtrekking geraak dat tussen 0.5 tot 5% van alle longkarsinome uit hierdie soort longtumor bestaan. Etlike etiologiese faktore is in oorweging geneem, ‚maar geen gemeenskaplike faktor kon gevind word nie.' Geen skuld kon aan virusse gegee word nie, en gesien die feit dat dergelike tumors ook by honde en skape aangetref is, is dit nie verrassend dat geen poging aangewend is om die rook van sigarette as die oorsaak van die kanker aan te dui nie.

LONGKANKER BY DIE MENS IN NIEU-SEELAND, SUID-AFRIKA EN DIE V.S.A.

'n Ander interessante kenmerk van die besprekings in Weenen was bevestiging uit Ohio van die werk waaroor Eastcott in Nieu-Seeland en Dean in Suid-Afrika verslag gedoen het. Die Ohio-studies het betrekking gehad op immigrante uit Engeland, Wallis en Italië wat hulle in Cuyahoga County, 'n intensief geïndustrialiseerde gebied, gevestig het. Die longkankersyfer onder die immigrante was veel hoër as onder die burgers wat in die betrokke dele gebore is; en tog was hierdie syfer veel kleiner as in die immigrante se land van herkoms. Haenszel (van die Nasionale Kankerinstituut) het die Ohio-bevindings getoets tydens 'n lands-

1. *Advances in Internal Medicine,* Deel X. Uitgawe deur William Dock & I. Snapper. 1960. Bl. 343. Chicago: Year Book Publishers, Inc.

As the cigarette smoking pattern of the foreign-born and the native-born is approximately the same, the inference is inescapable that the urban factor associated with lung cancer cannot be related in any important way to the smoking of cigarettes.

Equally striking is the fact that the higher incidence of lung cancer in males as compared with females was no longer found to obtain in Haenszel's study. If the smoking history is standardized for both sexes, the ratio is 3.6 : 1; but when foreign-born immigrant females are compared with immigrant males from Mexico, Norway, Russia, Sweden, Italy and Ireland, there is a reversal of this ratio. Such a reversal among foreign-born immigrants cannot be explained on the basis of cigarette smoking.

Dorn's prospective study on U.S.A. veterans based on insurance records indicated an association between cigarette smoking and coronary heart disease, lung cancer, oesophageal cancer, gastric cancer and prostatic cancer. The great ease with which almost anything can be blamed on cigarette smoking when statistical studies are relied on, must surely embarrass the proponents of the view that cigarette smoking causes lung cancer. Dorn's conclusions have not been confirmed, e.g. although cigarette smoking is twice as high in Whites as in non-Whites yet, in Ohio, the rate in non-Whites for oesophageal cancer is almost double that of the rate for White smokers. Burrows' work in South Africa indicates that there exist in the Transkei pockets with very high rates of oesophageal cancer in the indigenous population without any suggestion that this is related to smoking habits.

The Ohio study also showed an excess of gastric cancer among non-Whites as compared with Whites, although reversal should have been the case if cigarette smoking was an important aetiological factor.

Dorn showed one of the highest associations in his series between cancer of the prostate and cigarette smoking, yet the Ohio study showed a marked excess of prostatic cancer in the non-White group over the White group.

There is now a very formidable array of evidence, gathered from many quarters, which casts much doubt on the validity of the facile and much publicized hypothesis that cigarette smoking is an important cause of lung cancer. The attempt to blame everything on the cigarette has clearly been a vast over-simplification of a complex problem. Many different aetiological factors appear to be at work and scientific studies can only gain in value if they recognize the intricate variables involved.

wye studie van immigrante wat in die buiteland gebore en tans in die V.S.A. woonagtig is. Sy ontleding, gegrond op die bestudering van immigrante uit 12 lande, het aangetoon dat die longkankersyfer onder hierdie immigrante hoër was as onder burgers wat in die Verenigde State gebore is. Op 'n nasionale skaal gevestig dit dus die werk wat in Ohio, Nieu-Seeland en Suid-Afrika gedoen is.

Aangesien die sigaretrook-patroon van buitelandse en binnelandse geborenes min of meer dieselfde is, is daar 'n onontkombare gevolgtrekking, nl. dat die stedelike faktor wat met longkanker geassosieer is, in geen belangrike opsig met die rook van sigarette in verband gebring kan word nie.

Ewe opvallend is die feit dat die hoër voorkoms van longkanker onder mans in vergelyking met vroue nie vir Haenszel se studie gegeld het nie. As die rookgeskiedenis vir albei geslagte gestandaardiseer word, is die verhouding 3.6 : 1; maar wanneer buitelands gebore vroue-immigrante met mans-immigrante uit Mexiko, Noorweë, Rusland, Swede, Italië en Ierland vergelyk word, is daar 'n omkering van hierdie verhouding. Hierdie ommekeer onder buitelands gebore immigrante kan nie verduidelik word op die basis van die rook van sigarette nie.

Dorn se prospektiewe studie met Amerikaanse oorlogsveterane was op versekeringsyfers gebaseer en het aangedui dat daar 'n verband is tussen die rook van sigarette en koronêre hartkwaal, longkanker, slukdermkanker, maagkanker en prostaatkanker. Die uiterste gemak waarmee sigarette die skuld vir feitlik alles gegee kan word as 'n mens jou bloot op statistiese studies verlaat, moet die voorstanders van die sienswyse dat sigaretrook longkanker veroorsaak, reeds erg in die verleentheid gebring het. Dorn se gevolgtrekkings is nie bevestig nie; bv. hoewel die aantal sigaretrokers onder blankes byna twee keer groter as die aantal sigaretrokers onder die nie-blankes van Ohio is, kom daar byna twee maal soveel gevalle van slukdermkanker onder nie-blanke as onder blanke rokers voor. Burrows se werk in Suid-Afrika dui daarop dat daar in die Transkei ‚kolle' is waar die aantal gevalle van slukdermkanker onder die inheemse bevolking baie hoog is, maar hy doen nie aan die hand dat dit met die rookgewoonte in verband staan nie.

Die Ohio-studie het ook aangetoon dat daar veel meer gevalle van maagkanker onder nie-blankes as onder blankes voorkom, hoewel 'n mens net die teenoorgestelde sou verwag het as die rook van sigarette 'n belangrike etiologiese faktor was.

Een van die treffendste assosiasies in Dorn se reeks was dié tussen prostaatkanker en die rook van sigarette. En tog het die Ohio-studie bewys dat daar veel meer gevalle van prostaatkanker onder die nie-blanke groep as onder die blanke groep voorkom.

Daar is tans besonder oortuigende bewyse, ingewin in talle kringe, wat aansienlike twyfel werp op die geldigheid van die gemaklike en veel gepubliseerde hipotese dat die rook van sigarette 'n belangrike oorsaak van longkanker is. Die poging om die skuld vir alles aan die sigaret te gee, het heel duidelik op 'n geweldige oor-vereenvoudiging van 'n baie ingewikkelde probleem uitgeloop. Dit skyn asof talle verskillende etiologiese faktore aan die werk is, en wetenskaplike studies sal oneindig in waarde toeneem indien hulle erkenning aan die ingewikkelde veranderlikes wat by die saak betrokke is, verleen.

MEDICAL ASPECTS OF AIR POLLUTION*

AN INTERNATIONAL CONFERENCE

HELD IN VIENNA, 29 AUGUST 1960

Air pollution is usually thought of in terms of acute disasters such as occurred in the Meuse Valley, Donora and London. However, authorities now recognize that the effects of long-term exposure to low concentrations of atmospheric contaminants in the community and occupational environments are, perhaps, of greater medical significance than these dramatic episodes. Many physicians are showing increasing interest in the possible relationship of air pollutants to the diseases of their patients. In view of these considerations, Science Information Bureau—in accordance with its policy of serving education and research in medicine and those fields of science and industry related to public health—organized a conference on the increasingly important subject of air pollution at a uniquely appropriate time and place.

The Sixth International Congress on Diseases of the Chest of the American College of Chest Physicians, at the University of Vienna, 28 August to 1 September 1960, attracted an attendance from all parts of the world. This gathering of clinicians and investigators interested in cardiopulmonary disorders provided an outstanding opportunity for sponsorship by Science Information Bureau of an authoritative international conference on *Medical Aspects of Air Pollution*. This conference, held at the Imperial Hotel, Vienna, 29 August 1960, was attended by physicians with wide experience in diverse scientific disciplines. Their discussions were free and informal and from many viewpoints, including Medical Practice, Clinical Investigation, Public Health, Industrial Medicine, Biostatistics, Epidemiology, Pathology, Cancer Research and Biochemistry. The participants described their own observations, interchanged information, analyzed recent statistical, epidemiological and experimental findings and—most important of all—presented new ideas for research and education.

Dr. Andrew L. Banyai: I have been conducting conferences of this type for a good many years. Because of this, I have learned that the best way of getting all the benefit of your knowledge is by calling upon each of you in alphabetical order at the start.

THE PROBLEMS OF AIR POLLUTION

We are conferring upon a most fascinating subject. The annual economic loss in the United States due to atmospheric pollution is estimated to be about 1.5 to 4 billion dollars. Our lack of awareness of the importance of this problem is underscored by the fact that this year, in the face of several billion dollars of economic loss, only a few million dollars for research on the prevention of air pollution was appropriated.

There is, I believe, a psychological barrier of habituation. Because contamination of the atmosphere is not visible all the time, we take it for granted that it isn't there. Actually, there is an analogy with the era before bacteriology. We ignore it because we don't know. Therefore, I should like to hear your views as to what are the facts concerning air pollution in various parts of the world, and also your opinion about its effects upon the lung, the heart, the circulation, and other parts of the body.

I should now like to call on Dr. Alarcon.

Dr. Donato G. Alarcon: Many factors must be considered when we discuss air pollution and its effects. Man, confronting the multiple problems affecting his life, such as disease, accidents, social complexities, has a tendency to seek unique, simple causes. The discovery of bacteria as sufficient cause of specific diseases has led the scientific world toward the search for unique causes for all diseases, with wonderful results. But man, perhaps, has been led astray by this pattern of reasoning. We are after a unique bacterium or virus for each disease. Perhaps cancer is evading our efforts to clarify its etiology because our present thinking forces all reasoning toward a unique cause.

Why do we persist in the idea that, for instance, cancer of the lung should have a unique cause? Why must we consider cancer

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of the lung as one disease, and not, perhaps, a group of diseases? Even if its cause is unique, study of the large number of circumstances which favor its development is of importance. The cause could be a virus, but its successful implantation in human tissue is conditioned by some exacting conditions. Our awareness of the fact that fortuitous and perhaps multiple circumstances may be acting together, should stimulate our efforts to discover these, not too numerous, we hope, causes.

The observation of the relative immunity of certain groups to cancer of the lung must not be overlooked because, perhaps, the study of these human groups may give us the key to immunity. The search for multiple factors and the clarifying of their importance may achieve much in showing the circumstances associated with non-development of cancer and the measures needed to protect man. I believe that Pasteur gave us more by demonstrating the chicken's loss of resistance to anthrax when kept in an unfavorable environment than he brought us by his discovery of the germ.

Dr. Banyai: Thank you, Dr. Alarcon. I wish to flag time for all of us for the simple reason that we have many topics to discuss and comment on briefly. It gives me great pleasure at this time to call on Dr. Dean.

FINDINGS FROM 10-YEAR SOUTH AFRICAN STUDY

Dr. Geoffrey Dean: Mr. Chairman, I think most people here know about my preliminary South African research. As a consultant physician coming from Liverpool, where lung cancer is very common, I was surprised to find that not only I, but also other consultant physicians very seldom saw anybody with lung cancer. And yet cigaretes were cheap and most people were heavy smokers. Eventually I was so stimulated by this that I went into the matter and found that the white South Africans were the heaviest smokers in the world—heavier smokers than the men of the United States, who now rank second.

I went through the death certificates for a ten-year period and I checked the hospital records for these people. For the 10-year period that I studied, I found the lung cancer incidence less than half of that in Britain. Then I came across another phenomenon which I hadn't known about before I started my study. This was that the British immigrants to South Africa had a much higher lung cancer rate than the South African-born, particularly the age group 45 to 64 years.

The British immigrants, having spent the first 24 or 25 years of their lives in England, generally smoked less than the South Africans. I have since studied the smoking habits of the men who died of lung cancer by tracing their widows and sending them questionnaires when they were found. I also studied a group of controls obtained by taking the next death in the death certificate reports after a lung cancer death in which the man was in the same age and urbanization group. I found that the British immigrants smoked less before they came to South Africa and then increased their smoking to South African levels, but never exceeded the South African levels. Therefore, we had, first of all, the phenomenon that South Africans, the world's heaviest smokers, had a lung cancer rate that was less than half the rate in Britain. Secondly, British immigrants had a lung cancer rate that was 44% higher than the South African-born rate.

AIR POLLUTION AND LUNG CANCER IN DURBAN

Another phenomenon that came to light was that one city in South Africa, Durban, had a lung cancer rate that was higher than that of 2 bigger cities, Johannesburg and Cape Town. In Johannesburg and Cape Town are the main medical schools with the highest number of well-trained medical men and thoracic surgeons; and yet the lung cancer rate in those two cities was 50% below the rate in Durban. When I went into the air pollution question with the government officers I found that Durban had a very serious air pollution problem. It is a small Los Angeles. There is an air inversion phenomenon, so that the air does not rise and the smog stays on the ground. If you stand on the hills surrounding Durban it's hard to see the buildings in the centre of the town because of the smog.

As might be expected, the lung cancer rate for British immigrants in Durban was the highest of all groups in South Africa. It has actually reached the fantasic level of more than one in six of all male deaths between 45 and 64 years—that is nearly 20%. These deaths are well verified; the autopsy rates are high. The diagnostic levels in the big cities of South Africa are very good. There is no doubt that there really is almost an epidemic level of lung cancer in Durban.

Durban's air pollution compares with central London. Because of its peculiar geographical situation and air inversion phenomenon, the air pollutants produced by the factories and

the cars and the chimneys of Durban are trapped on the ground and do not rise and get away. I come from a city, Port Elizabeth, which is 600 miles from Durban and which is renowned all over the world for its wind. It's supposed to be the second windiest spot in the world. The smoke from our chimneys is rapidly blown to sea. Although we smoke as many cigarettes per head as the men in Durban, according to the Bureau of Statistical Survey our lung cancer rates are less than 40% the Durban death rates. As in Durban, however, the lung cancer rates are higher for British immigrants than they are for South African-born. This applies to all cities, other urban areas and even to the rural areas.

The second part of our research, which has not yet been published, is an analysis of the habits—taking the word habits in the widest sense—of the lung cancer patients, of the controls, who were the men who died but not from lung cancer, and also of a third group of men who are still alive in the same age and urbanization groups. The study has been successful to the extent that I managed to trace 55% of the widows of lung cancer patients and of the controls for the 10-year period. The lung cancer patients, on average, smoked more than the controls, an average of 32 cigarettes a day, as compared to 26 for the controls—6 cigarettes a day more. However, the British immigrants in the cities did not smoke more than the South African-born. In fact, they tended to smoke less before they came to South Africa and then their levels rose to South African levels.

Among the South African-born who died of lung cancer, 14% had visited Britain for an average of 4.3 years, while less than 8% of the controls had visited Britain. The British immigrants who came out at a later age tended on average to die of lung cancer at a younger age. For instance, those who died between the ages of 45 and 54, had immigrated at an average age of 30 years. And those who died between 55 and 64 had immigrated at the earlier average of 24 years. This differential did not occur in the controls—the men who did not die of lung cancer. In both age groups, 45–54 and 55–64, the controls immigrated at an average age of 24 years. So, the longer they stayed in Britain before they came to South Africa, the earlier they were likely to develop lung cancer. The peak of the incidence of lung cancer in South Africa is nearly 10 years later than it is in Britain.

My own conclusions and my own feeling about the results of this research are this: that there seems to be very strong evidence that lung cancer results from environmental factors and that it has not been primarily genetically determined; that it results, in fact, from the air we breathe. The air we breathe may be polluted socially or personally. If we are living in Los Angeles, there is a very heavy social pollution. If we live in Los Angeles and then smoke 50 cigarettes as well, we are increasing the risk probably. This seems likely to me from the evidence we have.

Dr. Banyai: It gives me great pleasure at this time to call on Dr. Eastcott.

Dr. David F. Eastcott: I have published figures from New Zealand which are similar, in essence, to those Dr. Dean reported from South Africa. Immigrants from the United Kingdom, when compared with people born in New Zealand, had a higher incidence of lung cancer. The incidence was higher among people who were relatively older at the time that they immigrated. It is, perhaps, unwise to suppose that this could be wholly explained on the premise of air pollution, although a lot of the epidemiological evidence suggests that there is such an explanation.

LUNG DAMAGE IN YOUNG IMMIGRANTS TO NEW ZEALAND

There is one fact which came out from the figures which I have, and that is related to immigrants who came to New Zealand when they were less than 35 years old. About a third of these were children under the age of 15 and the bulk of the remainder were in their early twenties. In this group there was quite a substantial increase, some 30%, in the chance of lung cancer compared to the New Zealand-born. It seems to me that these children of 15 couldn't have got a very big dose of carcinogen from the atmosphere. It appears that atmospheric conditions and crowding and so on in England had the effect of producing more chronic diseases in the lungs and that cancer then developed on the basis of some damage produced in childhood. I do not have the figures in support of this, for I am still working on them. There was a very substantial increase in post-mortem findings of chronic lung conditions in immigrants, even though immigrants are screened by X-ray before they come to New Zealand. There was a higher incidence of old scarring from tuberculosis and of chronic bronchitic changes. It seemed to me that conditions in the United Kingdom were more unfavorable and on the basis of that there was an increase of lung cancer.

Although it isn't a straightforward relation, I think it's well substantiated nowadays. My feeling is that this is an important finding.

I estimated the differences in smoking habits and I came to the same concluson that Dr. Dean came to. There is a slightly higher rate of cigarette smoking among New Zealanders than among English. New Zealanders have a habit of 'rolling their own,' so, when my figures relate to the amount of tobacco used for hand-rolled cigarettes, Dr. Doll seems to think that it be considered smoking a pipe. I am trying to convince him now that it is cigarettes.

Dr. Banyai: Thank you, Dr. Eastcott. It now gives me pleasure to call upon Dr. Farber, Past-President of the American College of Chest Physicians.

Dr. Seymour M. Farber: Thank you, Dr. Banyai. Perhaps one of the most important acute as well as chronic problems we have to do further investigation upon in the United States is the effects of air pollution on the health of our population. It is a privilege to hear the remarks of men such as Professor Alarcon, Dr. Dean, and Dr. Eastcott. I personally have not worked along these lines, and I know that later we will hear from one of our distinguished colleagues who has done extensive work in this field, Dr. Mancuso. I should like to wait until we hear from him.

Dr. Banyai: Dr. Flipse, who is the Incumbent President of the American College of Chest Physicians, knows a great deal about air pollution. Dr. Flipse, will you please comment now?

Dr. M. Jay Flipse: My only comment is that in Dade County, Florida, we have about the same incidence of bronchogenic carcinoma as Dallas, Texas—about 28 per 100,000 population per year. In Atlanta, Georgia, the incidence is perhaps 13 or 18. I don't have the exact figure, but I know that it is small. In New Orleans the figure is something like 42. These are all Southern cities, but there is a distinct difference among them in regard to industrial soots, smog, smoke and so forth. The incidence of industrial smoke in South Florida is practically nil.

Dr. Banyai: How about Central Florida, Dr. Flipse?

Dr. Flipse: The incidence in the central part of the state of Florida is exceedingly low. There is heavy industry in and about New Orleans that we do not have. The amount of coal burned in Florida is approximately one pound per person. That is exceedingly low compared with Britain and other countries. We have practically no smoke problem. Our electricity is produced by burning oil and there is practically no smoke produced by that.

Dr. Banyai: Do you have any air sampling stations in Southern Florida, Dr. Flipse?

Dr. Flipse: Yes, we have. But our sampling is largely related to automobile traffic on asphalt roads. There we have a high incidence of dust in comparison to other forms of air pollution. It appears that the peculiar statistical evidence on air pollution and its effects has as yet not been clarified, and that the mechanisms in one place may be different from the mechanisms in other situations.

Dr. Banyai: Thank you, Dr. Flipse, I should now like to call on Dr. Ibrahim.

Dr. Mohammed Ibrahim: Mr. Chairman, my experience is that of a professor of Clinical Medicine in East Pakistan, a country which is without any highways and without many automobiles. My interest in lung cancer was aroused in 1950 after the *First Conference on Diseases of the Chest* in Rome. I read a short paper on proven cases of cancer of the lung especially for the reason that lung cancer was prevalent even among people who never smoke cigarettes and from areas where there are very few automobiles. Now, there are naturally, I thought, other sources of air pollution. This led me to the next question of general air pollution affecting the health of our people.

AIR POLLUTION IN EAST PAKISTAN

Pollution of the air may cause non-specific and specific afflictions. Non-specific disorders are due to sudden changes in temperature, humidity, or barometric pressure, as happens in East Pakistan. Due to the north-western winds and the monsoon, there are sudden great changes in atmospheric conditions and humidity. This may cause an inhibtory effect on the ciliary movement of the bronchial mucous membrane —as in Professors Banyai's term 'broncho-peristaltic inhibition'—with bronchospasm, and cor pulmonale. These are fairly frequent and common in our part of the world.

Specific afflictions might be due to dust, which in rural areas is due to smoke, because of the people's habit of cooking their food in a thatched house without proper outlet. As to industrial air pollution, till 1947 there were very few industries in our country, i.e. only 392. By 1955 there were 419 and now, during the last 2 years, it has gone up to about 1,000. Now more industries are coming. Especially interesting are those which are due to a recently discovered gas containing

methane in one area of East Pakistan, changing the chemical environment. Other industries such as jute, cotton, match factories, flour mills and saw mills are producing changes in our physical environment. I think some of these, if we do some research work, may be found to be contributing to the changes in bronchial epithelium that may lead to lung cancer.

Dr. Banyai: Thank you very much, Dr. Ibrahim. And now it is a great pleasure to call upon Dr. Kaida.

AIR POLLUTION IN JAPAN

Dr. Katsumi Kaida: Mr. Chairman, I would like to briefly introduce results of air pollution studies in Japan. In Japan also, the atmosphere of cities, especially industrial cities, has rapidly come to be polluted as a result of recent industrial development. Air pollution has become recognized as a public nuisance. Consequently, surveys and studies of air pollution have become important during the past few years.

The most salient characteristic of Japanese air pollution is that it is mainly caused by combustion of low-grade coal by large industries. Emission of pollutants from residences is not great, except in Sapporo City. However, even within a single city, there are considerable differences in the degree of air pollution between the industrial section and the residential section. In Japan, such accidents as happened in the Meuse Valley and in London do not occur, probably because the major industrial cities are favorably located on the sea coast.

Now, the influence of air pollution on the human body has to be considered. The fact that Yokohama Asthma is cured by change of climate indicates the strong influence of air pollution. It is interesting that this asthma does not occur with greatest incidence around May, when the dustfall is greatest, but occurs more frequently in winter, when suspended dust and SO_2 are highest.

EFFECTS ON MORBIDITY AND MORTALITY

Nose and his co-workers investigated the daily mortality among citizens of Ube City and found that more patients died on the days when the wind velocity was low and the levels of suspended dust and SO_2 were high. They stated that it could not be denied that air pollution had a direct and indirect influence on mortality.

Nose and his co-workers also showed, by comparative studies of mortality by major causes of death in Ube and Bofu Cities, that infantile and senile mortality were higher in Ube City. They found the mortality rate from diphtheria to be 7.8 times higher in Ube City than in Bofu City—likewise, lung cancer mortality was 2.4 times higher in Ube City. Mortality from bronchitis, asthma and tuberculosis was especially higher in Ube City. The annual and the monthly trend of mortalities from pneumonia and bronchitis had a correlative relationship to dustfall as did diphtheria morbidity. In other words, there seems to be a close relationship between respiratory diseases, dustfall and climatic factors combined.

Saruta and his co-workers made a survey of health insurance patients in smoke-laden Yawata City and compared findings with Fukuoka City whose atmosphere contains little pollution. Their study showed that there was more pulmonary tuberculosis, asthma and inflammation of the upper respiratory tract in Yawata City than in Fukuoka. This suggests that air pollution exerts a chronic influence on the respiratory system rendering it susceptible to diseases.

Finally, the relationship between lung cancer and air pollution cannot yet be discussed decisively. However, the fact that lung cancer has recently been increasing rapidly in Japan and is particularly high in areas where the atmosphere is highly polluted, leads us to suppose that there is some influence of air pollution upon lung cancer.

RESEARCH PROGRAM IN YAWATA CITY

Therefore, I have developed the following research program. We have selected Yawata City in the Northern Kyushu industrial area where the atmosphere is highly polluted as a survey area. We plan to conduct periodic chest X-ray examinations and cytological sputum examinations on 30,000 citizens over 40 years of age for 5 years. The examination will be repeated on each individual each year. In the cytological studies, we will search not only for cancer cells, but also for indications of a precancerous condition in the bronchial epithelium. At the same time we will continue pathological examination of the lungs of persons who die of lung cancer and the resected lungs of operated patients.

Dr. Banyai: Thank you, Dr. Kaida. We will now hear from Dr. Mancuso.

U.S. FINDINGS CONFIRM SOUTH AFRICAN AND NEW ZEALAND STUDIES

Dr. Thomas F. Mancuso: First I'd like to comment on the work we have conducted in Ohio. We did a study in Ohio which confirmed the work of Dr. Eastcott and Dr. Dean. We studied the immigrants from England, Wales and Italy who came into Cuyahoga County, a highly industrialized county in Ohio. Without question, the lung cancer rates among the immigrants were much greater than among the native born of the 8 metropolitan counties of Ohio; and yet, it was much less than in the immigrants' country of origin. For example, the rate for the immigrants who came to Cuyahoga County from England and Wales was 31.75 per 100,000, whereas in the country of origin at the same time it was 55.48. So, in effect, we have confirmed what Dr. Dean and Dr. Eastcott have established.

Recently I had the opportunity to review an unpublished paper by Mr. Haenszel of the National Cancer Institute, and he has given me permission to quote from it. It has much bearing upon what we are discussing and I would like permission to comment on it.

Dr. Banyai: Certainly, Dr. Mancuso.

Dr. Mancuso: Haenszel tested our findings in Ohio and what was observed by Dr. Eastcott in New Zealand and Dr. Dean in South Africa. His national study of foreign-born immigrants in the United States is to be published as a monograph. I have analyzed it in considerable detail and it says, in effect, that foreign-born immigrants to the United States from 12 countries definitely do have a higher lung cancer rate than the native born of the United States. Without any question, this confirms, on a national basis in the United States, the work of Dean, Eastcott and myself.

Now, the next step in this study was to compare the immigrants from 5 countries—England and Wales, Norway, Sweden, Germany, Italy—with United States natives and those remaining in the country of origin. Here again Haenszel found exactly what Eastcott, Dean, and myself had found. Immigrants from England and Waies have a much higher rate for lung cancer than United States natives, but considerably lower than their country of origin. So, I think we can assume with a real degree of certainty that there must be some factor associated with the immigrants from England and Wales, as I and others think, a factor definitely associated with atmospheric pollution.

An additional observation in the study was that the smoking relationship between the foreign born and the native born is approximately the same. This is very important, because we found in Ohio that the foreign-born had a very high lung cancer rate compared to the native-born. Now, if the smoking pattern is approximately the same, it indicates that there is a foreign-born phenomenon in addition to the fact that, as pointed out, there is an urban factor.

There now comes into focus a so-called foreign-born factor. When immigrants from 12 countries were compared with U.S. natives, the incidence of lung cancer was found to be higher in immigrants from 8 countries and lower in immigrants from 4 countries. This does not tie in with the smoking theory concept.

VARIATIONS IN MALE : FEMALE LUNG CANCER RATIO IN U.S. IMMIGRANTS

But more striking is the fact that the male : female ratio disappeared in 6 of the countries. In other words, up to this time everyone has accepted the fact that there is a male : female difference in lung cancer rates—the ratio being given as 7 : 1 or 5 : 1. If smoking history is standardized for both sexes, according to Haenszel, the ratio is 3.6 : 1. However, when the foreign-born immigrant females are compared to males from 6 of the countries, the females have a higher ratio. This reversal of ratios occurred in immigrants from Mexico, Norway, Russia, Sweden, Italy and Ireland; and in immigrants from 3 countries the male : female ratios are approximately the same: England and Wales, Austria, Germany. And in immigrants from 3 countries the female lung cancer rates are less — Czechoslovakia, Canada and Poland. Now, these variations in ratios among foreign-born immigrants cannot be explained on the basis of cigarette smoking.

This opens up a whole new area for analysis and study. Haenszel acknowledges that there is an urban-rural difference and that there must be some phenomenon associated with the foreign-born which is not related to the fact that they are residents in an urban area. You see, we in Ohio have found that the foreign born not only have a higher lung cancer rate in the urban areas, but a much higher rate in the rural areas. So, very definitely, the urban-rural relationship cannot be explained by the fact that there are more foreign born living in the urban areas. The urban-rural compari-

son in regard to Denmark and Finland bears this out.

Dr. Banyai: Thank you, Dr. Mancuso. It now gives me great pleasure to call upon Dr. Ono.

AIR POLLUTION AND LUNG CANCER IN JAPAN

Dr. Jo Ono: The air pollution and lung cancer problem has become increasingly great in Japan. A recent newspaper article, *Smoke Problem in Tokyo Area Studied by Airplane Round Tokyo Tower*, shows that we are very much pollution-conscious. Now, I don't think I should go into statistics that you all know, but I do want to describe briefly some important findings.

In 1947 the mortality rate in Japan from cancer of the lung per 100,000 population was 1.2 in males and 0.5 in females. In 1950 it rose to 1.9 in males and 0.8 in females. In 1955, the rates were 4.3 in males and 1.8 in females. Now in 1958, there were in actual number 2,901 male deaths and 1,337 female deaths from cancer of the lung. From 1948 until the present the rate has increased in Japan about 4 times. Now, about the lung cancer mortality rates in different countries; Scotland, England and Wales are highest and Japan is lowest.

Now, here's our situation with regard to air pollution. The amount of dust deposited is considerable in our major industrial cities—Tokyo, Kawasaki, Yokohama, Sappora, near where we have coal mining, Kobe, Amagasaki and Ube. As much as 33 tons of dust per square kilometer per month are deposited in some parts of Japan. What does this indicate? It is related to lung cancer in that the Tokyo area has a death rate from lung cancer of 144—taking 100 as the average for the Japanese death rate. In Kawasaki and Yokohama the death rate is 120. The industrial cities, Sapporo, Ube and Amagasaki, also have high rates.

Here are findings advanced by Dr. Nose. The high content of dust in the air in Ube City seems to be responsible for a marked increase in incidence of certain diseases. In addition to the figures on diphtheria and lung cancer cited by Dr. Kaida, the incidence of heart disease is 1.2 times higher in Ube City, as compared with Bofu City, which adjoins Ube City and has a similar situation except that it has fewer factories. Air pollution and cancer and other conditions may have some relation.

Dr. Banyai: May I compliment you, Dr. Ono. Let us now hear from Dr. Pierson.

LUNG CANCER IN FRENCH IRON MINERS

Dr. Bernard Pierson: Mr. Chairman, we have been interested in the incidence of lung cancer in the iron miners of Lorraine, in France, and have had an opportunity to study a large number who presented themselves with various respiratory complaints. We selected the group of workers who usually cut the tunnels. All workers had had an exposure of at least 10 years and some, 20 years or more. In a series of more than 1,000 such workers we found an incidence of 3.3% of bronchogenic carcinoma. On the other hand, study of a similar number of mine employees whose duties do not require continuous exposure, such as clerks and engineers, showed an incidence of 1.5% bronchogenic carcinoma.

A second series of 2,000 miners was referred because of X-ray and clinical findings pathognomonic of pneumoconiosis. Importantly, the incidence of bronchogenic carcinoma was highest in the group with siderosis—1.8% compared with an incidence of 0.36% in the group with silicosis. What was surprising was the very high percentage of anaplastic carcinoma. While we had made the pathological diagnosis of anaplastic carcinoma in 30% of a previous series of 1,000 cases of bronchogenic carcinoma, in this study of iron miners we found 51% of the neoplasms were anaplastic carcinoma. We don't know why.

I would like to discuss another problem very briefly. It is about radon. We live in an atmosphere containing naturally occurring radioactivity in the form of radon. Radon is a gas we breathe in normal conditions without ill effect. But if we breathe radon in polluted air that contains dust, the radon will be adsorbed by the dust. Radon is not dangerous because its duration of life is only 3 days. But you have to remember that some by-products of radon are dangerous. There are many by-products, but their duration of life is very short—except for two. One is lead (Pb^{210})—its duration of life is 22 years and its product of degradation is polonium (Po^{210}). Its duration of life is 138 days, and its degradation product is alpha radiation—which is extremely dangerous if it is in contact with bronchial or alveolar cells. So we think radon is not dangerous, but if radon is fixed on dust, 22 years later it may be a producer of alpha radiation within the lung.

AIR POLLUTANTS IN MILAN

Dr. Banyai: Thank you, Dr. Pierson. Dr. Sirtori, would you please comment on atmospheric pollution?

Dr. Carlo Sirtori: With regard to air pollution, in 1956 we introduced a filter now installed in almost 3,500 heating and industrial plants. It consists of a cylinder through which a thin tube is passed in the central axis. The tube contains many small holes; it is closed at one end and water under pressure enters through the other to create an aqueous diaphragm. Combustion boiler smoke, passing through the cylinder, is 'washed' before being evacuated through the chimney. Solid and unburned particles fall and collect as a tar-like material. Ultraviolet spectrum analysis of this material, after extraction with benzol and chromatographic depuration, reveals benz-3, 4 pyrene. Each 100 kg. of carbon or naphtha yields 1 kg. of this tar-like substance which, in turn, contains about 20 mg. of benzpyrene. Since more than one million tons of carbon and naphtha are burned in Milan for winter heating, filters could collect 10,000 tons of tar-like material containing 2 kg. of benzpyrene.

We should like to point out specific industrial pollutants of importance, such as nickel, inorganic arseniates, chromates, beryllium, printing inks, isopropylic oils, iron dusts, and products of leather manufacturing.

Dr. Banyai: Are there any dust-fall counting stations in Milan?

Dr. Sirtori: Oh yes, there are.

Dr. Banyai: Are there any figures on how much dust is falling per month?

Dr. Sirtori: There are many, many papers on this subject, I think, as in London, in regard to air pollution. In Milan, there is great air pollution.

Dr. Banyai: In downtown Chicago there are months when we get as much as 126 tons of dust per square mile. Now we shall hear from Dr. Vorwald.

Dr. Arthur J. Vorwald: Our group has long believed that atmospheric pollution is a factor in the etiology of cancer of the lung. In this regard, however, I should like to relay to you a word of caution: rather than speak of air pollution, let us speak of air pollutants as a cause. For this reason, both our clinical studies and our research studies are directed to specific atmospheric pollutants. Let us not make the mistake of saying that all pollutants are responsible for cancer of the lung. Our interest lies in determining the atmospheric concentration of specific pollutants, the concentration in the lung of specific pollutants and the length of time that this material stays in what I call 'strategic segments of the lung.' We are also interested in the transport of a pollutant in the lung, and its elimination from the lung. All of these are extremely important in trying to identify the manner in which a pollutant might alter a cell and cause it to become cancerous.

STUDIES ON ACTION OF POLLUTANTS

In consequence, our studies are focused at the cellular level. We are now trying to find out the biologic activity of pollutants, single pollutants, pollutants inhaled together and pollutants inhaled one after the other. This leads us to the concept that there may be some pollutants which prepare the soil for other pollutant. Thus we speak of synergistic action and additive action—one pollutant may synergize another pollutant and thus provoke or cause lung cancer.

We are finding some very interesting and significant changes in the nuclei and in the cells in our biochemical studies of pollutants which we know are carcinogenic—methylcholanthrene, many of the higher hydrocarbons, beryllium. We are not as yet convinced that there is a relationship between siderosis and cancer of the lung. Let us realize that the man who is identified as a siderotic also inhales many other things. Probably, with clear-cut analysis, one will eventually be able to demonstrate that it is not the iron oxide that produces the cancer, but another component of the atmosphere which the siderotic inhales.

Furthermore, we are interested in the so-called absorptive phenomena of particles. We have, for example, a carbon particle or an iron particle in the atmosphere. Now, it can absorb gaseous components from the atmosphere and so act as a vector and localize a carcinogenic agent in a strategic segment of the lung, as in the case of the Schneeberg miners. While a particulate element of the atmosphere may absorb and retain a radioactive element at extremely low levels, it becomes high level radioactivity when this particle localizes in a cell which is susceptible to cancerous change.

Those are the problems with which we are dealing. But again, I should like to caution: let us think of pollutants rather than atmospheric pollution. By doing so, we will make progress in identifying the pollutants in our atmosphere which are responsible for cancer, emphysema, bronchitis and other disorders.

Dr. Farber: Dr. Vorwald, am I correct in recalling that about 70% of the miners exposed at Schneeberg developed lung cancer?

Dr. Banyai: 66% died of bronchogenic carcinoma.

Dr. Farber: While it is important to study this group carefully, equal consideration should be given to the 34% who were exposed and did not develop lung cancer.

Dr. Vorwald: That may be the most important group.

Dr. Farber: Perhaps this should be emphasized in all of our studies.

DO AIR POLLUTANTS CAUSE BRONCHITIS, BRONCHOSPASM, ASTHMA?

Dr. Banyai: Thank you, Dr. Farber. I am now going to pool 3 questions to save time. What are your opinions on the role of atmospheric pollutants in: the development of acute and chronic bronchitis; the development of acute and chronic non-allergic bronchospasm; and the incidence of bronchial asthma? Dr. Alarcon, can you give me your answers to these difficult questions?

Dr. Alarcon: Chronic bronchitis, bronchospasm and bronchial asthma are most prevalent where air pollution is most severe. They are much more prevalent in England than in other countries. In Mexico they are much less prevalent in the areas where we know the air is clear. In Mexico City, where I live, the air is becoming more and more polluted. We have a tremendous fall of dust in our city and we find that every year the cases of chronic bronchitis are increasing.

Dr. Banyai: Dr. Dean, would you please give us your comments on the influence of atmospheric pollution on the 3 diseases I mentioned?

Dr. Dean: According to the death certificates, Durban, which has a very high lung cancer rate, also has a bronchitis rate that is higher than that of any of the other cities. It is also well known for a tendency to bronchial spasm. In other words, the city that has a high lung cancer rate is also the city that has the bronchitis and asthma problem.

Dr. Banyai: Thank you very much. Dr. Eastcott, will you comment on this subject?

Dr. Eastcott: Atmospheric pollution, as produced in England and Wales by coal burning, is a potent factor in producing chronic bronchitis. That is borne out by the epidemiological studies of Reed and the work of Stocks and Dietrich relating to atmospheric conditions in cities. I think that it must, either directly or indirectly, account for some of the increase in lung cancer in England and Wales.

As to experiments, you can use atmospheres you get in the fog or smog and you can do physiological experiments over a period of hours or a day. I feel that you cannot make worthwhile deductions from these as to what might happen to a person exposed to air pollution in an area over a period of 20, 30 or 40 years. Physiological studies, so far as asthma and bronchospasm and so on are concerned, are, I feel, perhaps not helpful in deciding what the long-term effects of atmospheric pollution may be.

Dr. Banyai: Dr. Farber, would you give your comments, please?

Dr. Farber: We have some clinical and laboratory evidence on this in San Francisco, where we have studied a group of breathless patients during the entire year. We noted that the usual medications given for bronchodilation to this group were not so effective when the oxidant level of the atmosphere was raised. We found that our breathless patients required increased amounts of medication at the times of increased air pollution.

Dr. Banyai: Thank you very much. Dr. Flipse, will you speak about air pollutants and bronchitis, bronchospasm and asthma?

Dr. Flipse: We have a situation in Miami which is peculiar to South Florida. Periodically, in the dry season of the year, the Everglades catch fire. The Everglades are a peat bog and the acrid smoke which results from this burning occasionally drifts eastward, although the Trade Winds normally prevail and blow that smoke westward. When the smoke drifts eastward our asthmatics become acutely affected and develop aggravation of symptoms.

Dr. Banyai: As we can see, we have to keep in mind not only carcinoma of the lung when we discuss atmospheric pollution, but 3 additional diseases. May I emphasize at this time that there has been very little research work done on what we may call idiopathic bronchospasm. I wish some of the brilliant participants in this discussion would consider doing some original research work on non-allergic bronchospasm. It would be very helpful. And now may we hear from Dr. Kaida?

Dr. Kaida: I have studied the influence of different dusts on the respiratory system. The pathologic changes they cause are quite different, as you know. For example, the effect of free silicates, asbestos, beryllium and others is quite different. I have heard that cadmium also causes changes in the pulmonary tissue, but in a much different way. It first affects the vegetative nervous system, resulting in dystrophic changes of pulmonary tissue.

Dr. Banyai: Dr. Mancuso, if I am not mistaken, nobody has so far mentioned ozone, sulfuric acid and hydrochloric acid. Would you care to add your comments?

BERYLLIOSIS AND ASTHMA FROM AIR POLLUTION

Dr. Mancuso: I do believe that atmospheric pollutants contribute to chronic bronchitis in view of my own experience with certain epidemiological studies conducted in the working environment and the community environment. I was fortunate to conduct the epidemiological study on beryllium which, in 1948, established for the first time the incidence of berylliosis among neighborhood persons residing in the vicinity of a beryllium-producing plant. This established, without question, the first chronic lung disease which individuals could develop following low exposure to a certain chemical. We had another experience similar to this, in regard to chromate workers, that showed that chemical asthma can result from atmospheric pollution. In addition to the study within the plant, we made observations on one person who gave a history of allergy to chromates. We took him outside the plant quite a distance away, and started walking him toward the chromate ore pile. We were prepared and had the company physician and nurse ready with a hypodermic. As we approached the chromate ore pile, to within about 50 feet, he went into acute spasm and we had to give him medication.

Evidence of bronchitis due to working exposure has been recorded in the literature. Stokinger has done considerable work in regard to ozone. He has produced lung changes and fibrosis in animals subjected to ozone.

SYNERGISM AND ANTAGONISM OF POLLUTANTS

At this point, I should like to make a special plea for consideration of the total complex of the community aerial environment, the total complex of air pollutants. I do not believe, really, that we should be looking for one, or two, or three specific types of air pollutants which may be responsible for all these phenomena. The total complex acts in many different ways upon the human body, so that it is not possible to define just one effect on one single organ. I cite the experimental work done by Stokinger and others, including Amdur, which has shown the synergistic effects Dr. Vorwald referred to. Then there is the antagonistic effect to consider. You can take welding fumes and oxides of nitrogen which are acidic and which are liberated in the course of welding, but the presence of basic iron oxide will reduce their effects. Then the opposite, potentiation, as shown by Amdur. Sodium chloride and 2 parts per million of sulfur dioxide, can produce a tremendous potentiating effect, one that is greater than 70 parts of sulfur dioxide alone. Since so many of these phenomena are beginning to be understood, I, for one, would like to reserve judgment in regard to single air pollutants. I believe that all the various complexes act in certain ways which we do not understand at the present time, but undoubtedly affect the respiratory system.

Dr. Banyai: Dr. Ono, will you add to this?

Dr. Ono: Experimental studies carried out by a member of our University showed that the growth of mice breathing polluted air was retarded when compared to mice breathing filtered air. It was assumed that the smaller particles of vapor containing sulfur dioxide rather than the comparatively large particles of city dust were responsible for lung tissue changes. Histological changes were more apparent in the bronchiolar tissues than in any other part of the lung. The changes were generally of a chronic type. Practically all the mice breathing polluted air showed proliferation of the epithelium of the bronchioles. Epithelial proliferation was particularly marked in 16%. Also, emphysema was noted in 75% of the mice breathing polluted air.

Now, about Yokohama Asthma, first described by U.S. Army personnel. It really is bronchial asthma localized in the Yokohama area. Investigation of the air showed that contaminants during smog-free days amounted to 0.011 mg. per liter. During smog formation this increased almost 8 times to 0.081. The dust index on smog-free days was 1 and on the days of smog formation 3.8. Sulfur dioxide, ozone and nitrogen oxide levels were elevated on days of smog formation.

Dr. Banyai: Obviously there is a direct relationship between increased air pollution and so-called Yokohama Asthma.

Dr. Ono: It does appear to be so, Doctor.

Dr. Banyai: May I call on Dr. Pierson now concerning bronchitis, bronchospasm and asthma?

Dr. Pierson: As a pathologist, I am impressed by the modification of the epithelium of the bronchial mucosa that I see, and I am surprised there is not more carcinoma of the lung.

Dr. Banyai: Dr. Sirtori, would you please comment?

Dr. Sirtori: In my opinion there is tremendous air pollution in Milan, but bronchospasm, asthma and chronic bronchitis are not so frequent. I think it depends on the dry climate.

Dr. Banyai: Does Milan have a dry climate?

Dr. Sirtori: Yes.

Dr. Banyai: That's very interesting because the 3 conditions we are discussing are far more prevalent along our sea coasts—the gulf, the east coast and the west coast—and in the central part of the United States. So, what Dr. Sirtori said is very amazing information. Dr. Vorwald, may we hear from you?

Dr. Vorwald: First I wish to say that I agreed wholeheartedly with my colleague, Dr. Maneuso, when he mentioned that we should consider all atmospheric pollutants working together. And now, in respect to bronchitis, bronchospasm and bronchial asthma. I don't think there is any doubt that atmospheric pollutants do cause each and every one of these conditions. I think it is important, however, to know whether we are dealing with organic or inorganic pollutants in the causation of the various conditions. Finally, I must confess, gentlemen, that I have great difficulty in identifying clinically and getting my clinical colleagues to identify and to give the criteria for chronic bronchitis. What is chronic bronchitis?

DO AIR POLLUTANTS CAUSE HEART DISEASE

Dr. Banyai: Thank you, Dr. Vorwald, I want to ask Dr. Alarcon about the etiologic influence of atmospheric pollution on heart disease. Do you realize, Dr. Alarcon, that chronic bronchitis alone is capable of causing chronic cor pulmonale, and if that is the case, don't you think that there is a direct possibility of a connection between atmospheric pollutants and cor polmonale?

Dr. Alarcon: I certainly do.

Dr. Banyai: I would like to point out that there are some very eminent pathologists here who will back me up when I say cor pulmonale is secondary to chronic bronchitis. I would like Dr. Dean to comment on this.

Dr. Dean: Now in church, in the cinema or in the theater in England you will hear nothing but cough, cough, cough. Most of these people haven't got a bronchiectasis. They've got a chronic irritation of their bronchi, and this is called, in general usage, chronic bronchitis. They are bringing up a semi-purulent sputum half the time, and always blowing their noses. Now, this does not occur in South Africa. We've got a group of people who are also Western Europeans and when you go to the theater or a symphonic concert it's quiet.

In Durban, it's not the same. Durban has a bronchitis problem. There might be a difference in death certificate analysis as to what is a death from chronic bronchitis. Nevertheless—although this is not very statistical—it is interesting that the same type of doctor makes the diagnosis of chronic bronchitis more frequently in Durban than in other cities. They're the same type of men, they move around the country and they've been trained in the same medical schools. When a person has been coughing for 40 years and has cor pulmonale and dies, they put him down as a case of chronic bronchitis.

Dr. Banyai: Does he die of bronchitis or emphysema?

Dr. Dean: The death certificates are never simple. They will tell you: '*Cause of death;* cor pulmonale; contributing factors; chronic bronchitis and emphysema.'

ROLE OF AIR POLLUTION IN EMPHYSEMA AND COR PULMONALE

Dr. Banyai: Do you feel that air pollution may have a very definite role in the development of right heart failure?

Dr. Dean: Yes, of course.

Dr. Banyai: Dr. Eastcott?

Dr. Eastcott: I'm sure that is so, and I'm sure that cor pulmonale is much more common in those areas where there is a higher rate of chronic bronchitis. I feel that when you've got right heart failure, it's rather academic to discuss how you're going to describe the conditions in the lung which have given rise to it, and which is one more thing that has led to the death.

Dr. Vorwald: May I ask a question?

Dr. Banyai: Certainly, Dr. Vorwald.

Dr. Vorwald: In other words, you are saying that, in a patient with cor pulmonale, it is relatively insignificant to determine whether the col pulmonale is due to chronic bronchitis *per se,* without emphysema, or whether it's due to so-called obstruction of the airways with resulting emphysema, or emphysema along with increased intrapulmonary tension.

Dr. Eastcott: I'm only saying it's irrelevant to discuss what name you are going to put to it. I think you know, Dr. Vorwald, that when the doctor puts chronic bronchitis on the death certificate, what he is really thinking is that he's known the chap has been coughing for many years.

Dr. Vorwald: Yes, but it seems extremely important to me to determine whether a man can develop cor pulmonale or increase in pulmonary tension with chronic bronchitis alone, or whether it must be associated with emphysema.

Dr. Dean: I think it nearly always is associated with emphysema in the later stages.

Dr. Banyai: May I respectfully disagree, gentlemen? I know from my personal experience that there is such a thing as cor pulmonale secondary to chronic bronchitis, and I wish to go on record to this effect. Dr. Flipse?

Dr. Flipse: I question whether death certificates with the diagnosis of chronic bronchitis are specific or meaningful. As clinicians we recognize chronic bronchitis, but believe it to be a poorly defined, non-specific symptomatic diagnosis. The only way we define chronic bronchitis is by the symptom of cough. Our pathologists are not able to tell us that a given individual had chronic bronchitis. I do feel, however, that there is a definite relationship between chronic cough, irrespective of its etiology, and pulmonary emphysema.

Dr. Banyai: May I interrupt you just a second? Are you referring to the experimental clinical studies of Dr. McCann of Rochester, New York? He measured the intrapulmonary air pressure during cough and found that during strenuous coughing the intrapulmonary air pressure may go as high as 300 mm. of mercury above atmospheric pressure. I believe this is a terrific resistance for the right ventricle to overcome. It is no wonder, therefore, that anyone with a chronic cough of several decades' duration will sooner or later develop right ventricular degeneration.

Dr. Flipse: The question that you develop is again not clearly defined. You believe the increased pressure of the cough has a bearing upon the pulmonary circulation, causing overload of the right ventricle. I am inclined to think that the chronic cough causes pulmonary emphysema which diminishes the pulmonary vascular bed. This causes chronic increase of pulmonary vascular pressure. It is this, rather than the sudden explosive high-pressure cough, which causes the trouble.

Dr. Banyai: There is no doubt in my mind you are correct, that the largest percentage of cor pulmonale cases are secondary to what I call pseudohypertrophic emphysema and what others call idiopathic. The highest percentage of cases of cor pulmonale is secondary to this type of emphysema. But my point is this—chronic bronchitis of several decades' duration is bound to cause cor pulmonale because of intrapulmonary hypertension. Now let's call on Dr. Ibrahim.

Dr. Ibrahim: Etiologically, I believe, chronic bronchitis is due to factors such as air pollution or bacteria. Pathologically it is characterized by round-cell infiltration in the bronchioles and degenerative changes of the bronchial epithelium with destruction of the pulmonary vascular bed, followed by right heart failure with dilation of the right heart. It is one of the problems in East Pakistan where cases of chronic bronchitis, as well as emphysema and bronchial asthma, are frequent.

Dr. Banyai: Dr. Mancuso.

Dr. Mancuso: I'd like to make several points. First, I'd like to mention that the definition of chronic bronchitis in Great Britain and in the United States is entirely different. Second, I should like to caution against the use of what is recorded on death certificates as a cause of death in regard to bronchitis. One other point on bronchitis: there is definite need for an epidemiological type of study—a morbidity study. Bronchitis, I think, would be extremely difficult to evaluate on the basis of mortality. Now, in regard to cardiovascular effects of air pollutants, I have had no personal experience except for the beryllium study in which neighborhood cases who developed berylliosis also developed cardiovascular disorders.

Dr. Banyai: Dr. Pierson, please.

Dr. Pierson: In our work on the incidence of carcinoma of the lung in iron miners we made a statistical study of coronary disease, and there was no high percentage.

Dr. Banyai: And now, Dr. Sirtori.

Dr. Sirtori: I think that chronic bronchitis, emphysema and cor pulmonale are links of the same chain. I should like to note that electron microscopy has revealed a clear difference between atrophic emphysema and hypertrophic emphysema. The major difference lies in the alveolar basal membrane.

Dr. Banyai: Thank you very much. Dr. Vorwald?

Dr. Vorwald: I do not adhere to the view that chronic bronchitis *per se* can cause increased pulmonary tension which will lead to cor pulmonale. I think that in the majority of instances it is the diffuse emphysema—the changes in the pulmonary parenchyma with its attending changes in the septal capillaries—which produces the increased pulmonary tension and cor pulmonale. I believe that such pollutants as beryllium, which produces a diffuse interstitial pneumonitis, obliterating and obstructing the septal capillaries, can cause increased intrapulmonary tension and cor pulmonale.

I have seen cases clinically diagnosed as chronic bronchitis without emphysema, chronic bronchitis without cor pulmonale. Now, if the incidence of chronic bronchitis is high, and chronic bronchitis—without chronic bronchiolitis and emphysema—does lead to cor pulmonale, then I would expect a large increase of cor pulmonale in the general population.

Dr. Banyai: Thank you, Dr. Vorwald. Dr. Pierson, do you think that chronic bronchitis together with emphysema is a possible occurrence as a result of atmospheric pollution?

Dr. Pierson: Yes, in part.

Dr. Banyai: Dr. Ono, what do you think about the relationship between emphysema and atmospheric pollution?

Dr. Ono: I think that there is a definite relationship.

Dr. Banyai: Dr. Mancuso?

Dr. Mancuso: In regard to emphysema, I'm inclined to believe that there may be a relationship between supplementary effects of occupational and atmospheric pollutants. The few data that are available show a marked difference between males and females in mortality from emphysema. Again, I don't recognize this as valid because of its obvious limitations, but it's the only information we have in the United States. Yet, because of the tremendous difference between males and females, I am inclined to think that the occupational environment may be contributing significantly. So, one would assume that chronic bronchitis can be produced by atmospheric pollution and emphysema can develop from chronic bronchitis. I definitely feel, however, that we must give important consideration to the occupational environment.

Dr. Banyai: Dr. Kaida, what about emphysema?

Dr. Kaida: Most people think the cause of emphysema, especially obstructive emphysema, is bronchitis.

Dr. Banyai: Dr. Ibrahim?

Dr. Ibrahim: I think that bronchitis is definitely related to air pollution, but there is a significant group of emphysema patients in whom there is no sign of bronchitis.

Dr. Banyai: Dr. Flipse?

Dr. Flipse: I think that air pollution unquestionably complicates emphysema, as we speak of it clinically. But, you can have emphysematous lungs that have no obstructive features and emphysematous lungs that have considerable obstruction. There is the senile type of emphysema without impairment of pulmonary function. I believe that you have to define the question more exactly.

Dr. Banyai: For the moment, we are talking about what is generally known in the books as genuine emphysema, but I prefer pseudohypertrophic emphysema in contrast to senile emphysema. Let's omit senile emphysema.

Dr. Flipse: There's no doubt in my mind that air pollutants increase emphysema by way of cough, bronchospasm and asthma.

Dr. Banyai: Dr. Farber?

Dr. Farber: In many respects, in our discussions of emphysema, we're currently in the same position as, perhaps, 10 years ago, when we were discussing lung cancer. Was there actually an increase in lung cancer, or was it because of statistical methods? We have an overwhelming problem facing us in the coming years in dealing with patients with emphysema. Our considerations of etiology are overshadowed now by many factors, including our hesitancy to evaluate these factors. But, at the present time, if we are hesitant in agreeing upon etiology, I feel that there is no hesitancy in our stating that cough is bad for emphysema and that anything in the air that increases cough, increases the hazards of the emphysematous patient.

Dr. Banyai: Thank you very much. Dr. Eastcott?

Dr. Eastcott: I think coal burning is an important factor in producing trouble. It is coal smoke that is the principal factor in the increased incidence of chronic lung disease in such areas as England, Wales and Belgium.

Dr. Banyai: Dr. Dean?

Dr. Dean: I think most practising physicians are quite convinced, even if they haven't got statistical evidence for it, that air pollution, aggravating chronic cough, increases emphysema. We are, nearly all of us, inclined to advise our heavy smoking emphysematous patients to cut down their cigarettes, because we know that the chronic cough produced by heavy smoking is going to increase their emphysema.

Dr. Banyai: Dr. Alarcon?

Dr. Alarcon: I believe that emphysema is aggravated by air pollution once it starts, and it might start with a so-called dry bronchitis or wet bronchitis.

Dr. Banyai: Dr. Alarcon, I recently attended a lecture and saw photographs of Mexico City where automobiles were being driven with the lights on in mid-day. What was the reason?

Dr. Alarcon: Dust from the area around Mexico City.

Dr. Banyai: Would you call it atmospheric pollution?

Dr. Alarcon: In a way, yes, but a less harmful form of pollution. It's only vegetable earths, dust from the surrounding area.

Dr. Banyai: Incidentally, would you care to comment now on the effect of air pollutants on the eyes and the skin?

Dr. Alarcon: In our country the eyes are not affected.

Dr. Banyai: Dr. Dean, about irritation of the eyes by air pollutants?

Dr. Dean: I haven't come across personally, but I've read about the irritation to the eyes that occurs in Los Angeles. I know that certain vegetable spores can irritate the eyes at certain seasons of the year. I am sure that there are pollutants that do irritate the eyes and the nose.

Dr. Banyai: Dr. Eastcott? Skin, eyes, nose so forth?

Dr. Eastcott: Coming from New Zealand at the beginning of the year, I did notice the first few days I was in San Francisco that my eyes smarted and my nose was affected. I put it down to the petrol fumes and it cleared up after a few days.

Dr. Banyai: This is, incidentally, a very interesting statement because I have read that there is such a thing as developing tolerance to air pollutants. Am I correct about that? Has some animal experimentation been done?

Dr. Eastcott: Yes, that's so.

Dr. Banyai: May I ask a question of you, Dr. Flipse? How about natural gas as an air pollutant?

Dr. Flipse: I don't think it causes irritation.

Dr. Banyai: I mean, of course, the products of incomplete combustion.

Dr. Flipse: The products of incomplete combustion, yes, but not as great as fumes which contain sulfuric acid.

Dr. Banyai: Isn't the use of natural gas increasing in Florida?

Dr. Flipse: Yes, we use a great deal.

Dr. Banyai: Do you think there is a possibility that, as time goes on, incomplete combustion products of natural gas may cause a serious air pollution problem?

Dr. Flipse: I don't think so. The prevailing Trade Winds in our area do not predispose to concentration of these gases.

Dr. Banyai: Would you say that air pollution danger exists in valleys and geographic locations where there is no wind ventilation?

Dr. Flipse: That is, I believe, a very important factor. Where the topography is conducive to stagnation so that automobile exhausts and other fumes fail to clear, you have a great degree of trouble, as in Los Angeles.

Dr. Banyai: Dr. Ibrahim?

Dr. Ibrahim: There was an explosion in a gas field in East Pakistan in a valley bordered by hills. Just afterward, there were many cases of irritation of the mucous membranes of the eye and the nose.

Dr. Banyai: Dr. Mancuso?

Dr. Mancuso: To answer your question specifically, we have personal experience in Ohio outside of a steel plant which was liberating hydrogen sulfide. The sulfide united with the paint on the houses to form lead sulfide and blackened the houses. The people in the neighborhood developed nausea and vomiting.

In regard to the question about other organs that may be affected, this is one of our areas of weakness. We know very little about the long-term effects of low concentrations of air pollutants on humans. This is one of our biggest problems.

Dr. Banyai: May I say that your last statement should be underscored. The medical profession, as well as the public, is entirely forgetful of it. Please go ahead.

Dr. Mancuso: The toxicological effects are not known for one. Secondly, atmospheric pollutants *per se* do not produce a characteristic picture and this makes it very difficult to determine what is due to atmospheric pollutants and what is due to something else. We were fortunate in regard to beryllium, in the sense that there was more or less a characteristic type of X-ray finding in the chest which made it possible to screen out the people affected. But when you're dealing with atmospheric pollutants which do not produce a characteristic clinical syndrome it is very difficult to determine what is due to air pollutants and what is not. I would predict that, in the future, what we may learn within the occupational environment in regard to long-term effects—whether relating to lead, manganese, nickel, and so on, which are also in the general atmosphere—may then be applied generally. Do you want me to comment on tolerance?

Dr. Banyai: Yes, definitely.

CAN TOLERANCE TO AIR POLLUTANTS DEVELOP?

Dr. Mancuso: The recently reported work of Dr. Stokinger on mixtures of oxidant smog is, I think, quite important. It conveys the idea that we are dealing with many mechanisms which we are just beginning to understand. For example, he has been able to develop—and this work has been confirmed by others—a protective tolerance to ozone. He has exposed rats and others have exposed mice and rabbits to ozone. When these animals were re-exposed to ozone they showed a protective tolerance to the second exposure. Dr. Stokinger believes that this explains why, in Los Angeles, they have not noticed more effects when their oxidant level exceeds 0.55 parts per million.

Dr. Stokinger's experimental evidence shows that if you take an animal and expose it for 4 hours to 2 parts per million of ozone,

the animal is protected against a subsequent multi-lethal dose of ozone of 19.2 parts per million. He has also demonstrated what he calls a cross tolerance. He has taken a series of about 4 or 5 oxidants and shown how they can protect against one another. This is all occurring in the atmosphere in regard to people. He has also demonstrated the protective effect of oil mists, which protect against a subsequent exposure to nitrogen oxides and ozone. Finally he also has shown the synergistic effects of definite chemicals. This was in regard to hydrogen peroxide, 1.5 parts per million, plus 0.1 part per million of ozone, which actually produced some deaths in animals. Yet it takes virtually 200 parts per million of hydrogen peroxide alone to produce similar deaths. This was definitely a synergistic phenomenon.

With all these different possibilities I come back to the point that I made initially. I see air pollution as a total complex of the environment because we don't know which chemicals react with others to affect the human body.

Dr. Banyai: Dr. Ono, would you be kind enough to discuss briefly the incidence of carcinoma of the esophagus and stomach in Japan.

CANCER OF ESOPHAGUS AND STOMACH IN JAPAN

Dr. Ono: The following may be considered to contribute to the high incidence of cancer of the esophagus and stomach. First, Japanese, in general, like to eat piping hot food, and they're rice eaters. That is an unbalanced diet. In order to make up protein, fat and other factors, they have to eat large quantities of rice. The whole meal may be eaten in the course of 3 minutes. I found defective teeth in many cancer cases. In addition, we are sake drinkers and the sake must be hot. My series shows that 95% of the cases of cancer of the esophagus were sake drinkers.

Dr. Flipse: And what per cent of Japanese people drink sake?

Dr. Ono: Practically all men.

Dr. Flipse: All men? You have here two situations. One is that they all drink sake, and another is that 95% of those who have cancer of the esophagus drink sake. It does not prove anything.

Dr. Ono: No, it does not prove anything.

Dr. Mancuso: May I add to this?

Dr. Banyai: Please do so.

Dr. Mancuso: I should like to review several of the points I have come up with on the reported association between cancer and cigarette smoking, and see what you might think of them. First—and this stems from my own work and the work reported by Haenszel—I'd like to refer to 3 cancer sites: cancer of the esophagus, cancer of the stomach, and cancer of the prostate.

Now Dr. Dorn conducted a prospective study on veterans based upon insurance records. He found an association between cigarette smoking and the following items: coronary heart disease, cancer of the lung, cancer of the esophagus, cancer of the stomach, and cancer of the prostate. Now, in view of the information that I have and the information that I have derived from Haenszel's study there appear to be some inconsistencies which I'd like to bring out. For example, in regard to cancer of the esophagus, with which Dr. Dorn has stated that cigarette smoking is definitely associated, I should like to call attention to the fact that this has not been substantiated in Ohio and I do not believe that it has been substantiated in the study that Haenszel has done. This is the reason: cigarette smoking is twice as high in whites as in non-whites. In other words, for age 45 and over, the whites smoke twice as much observation, this would mean, therefore, that as the non-whites. On the basis of Dorn's cancer of the esophagus should be high among the whites. But just the opposite was the case in the study that we conducted in Ohio, comparing the white against the non-white. The non-white cancer of the esophagus rate was much greater than the white rate. Actually, the rate was about 19.9 : 10.

Secondly, in regard to the study Haenszel did on foreign-born immigrants from 12 countries, remembering again that the immigrants and the native whites have the same smoking habits. Males from all 12 countries had a higher rate for cancer of the esophagus than the native whites of the United States. We have the same problem in regard to cancer of the stomach since another inconsistency develops in regard to that. In our study in Ohio the non-whites showed an excess for cancer of the stomach over the whites, although the reverse should be the case, based upon smoking. The rate was approximately 60 *versus* 34 per 100,000. And then once again, the foreign-born immigrants from all 12 countries showed an excess against the U.S. males, and the same thing in regard to the females.

We have the same phenomenon in regard to the prostate. Once again, in our Ohio study, the non-whites showed a marked excess over the whites for cancer of the prostate, yet cancer of the prostate was one of those reported by Dr. Dorn to show one of the high-

est associations with cigarette smoking. Based upon the information I have at the present time, these inconsistencies lead me to question a number of the associations which have been developed.

ADVERSE EFFECTS OF AIR POLLUTION ON THE OLD

Dr. Banyai: I should like to address my next question to Dr. Pierson. Is it true that old people say 50 years and older, are more likely to suffer from atmospheric pollution than younger people?

Dr. Pierson: Yes, it is.

Dr. Vorwald: Dr. Banyai, don't you think that as we grow older we are less able to tolerate challenges? We are less able to withstand heat, the challenge of climbing stairs and the challenge of the insults imposed by atmospheric pollutants as we grow older.

Dr. Banyai: Of course. And since 10% of the population of the United States is 65 years of age or older, I believe the geriatric implications of the air pollution problem demand immediate attention.

Dr. Vorwald: In older people the total cardiorespiratory system is less able to meet the challenge of atmospheric pollutants. Their cleansing mechanism is below par, the filter capacity of the upper respiratory system is decreased, they already have a bronchial impairment. Furthermore many have an emphysema. The challenge of air pollutants superimposed upon an emphysema of another etiology is just the straw that breaks the camel's back. May I comment on the systematic changes?

Dr. Banyai: First, let's permit Dr. Sirtori to comment.

Dr. Sirtori: I think that the fundamental question is a cellular question. In the geriatric, you can see reduction of mitochondria, ATP, and so on. I think the reduction of mitochondria signifies reduction of oxidation in the cells. Reduction of ATP signifies the reduction of ciliary motion.

Dr. Vorwald: Yes, I think that our total repair mechanism declines as we grow older. Take, for example, fracture of the hip in the old, how long it takes to repair. Our total repair mechanism is gradually disturbed as we grow older—cellular replacement, which fits in with your thesis, Dr. Sirtori, namely, mitochondria, cell division.

With respect to the systematic changes provoked by atmospheric pollutants, we agree with Dr. Mancuso. We can cite many instances where the pulmonary deposition of an atmospheric pollutant in high concentration produces definite systemic changes—lead, manganese, beryllium, vanadium, the higher hydrocarbons, silver. But the real problem is that we do not know what a given pollutant at very low concentration in the atmosphere will do to the biological system over a span of 50 years. We just don't know.

HOW CAN WE INCREASE AWARENESS OF AIR POLLUTION?

Dr. Banyai: Gentlemen, we'll have one more round. I should now like to ask how we can approach the challenge of educating the medical profession and the public to make them air poilution conscious. Also, what orientation should we follow in the way of applicable research work?

Dr. Farber: Could I suggest, first of all, that Dr. Alarcon's paper given in Tokyo in 1958 be distributed to every physician.

Dr. Banyai: I second the motion.

Dr. Alarcon: I believe that this dangerous situation should be publicized and that the medical profession should be kept aware of it. And I would suggest also that we take preventive measures. One of them is that when we build new areas around a city the possibilities of air pollution should first be considered. The orientation of the place and the movement of air should be considered.

In Acapulco, there was this port surrounded by mountains. One of the old Viceroys of Spain, finding that the area was polluted and very hot, cut through the mountains to let air enter. That's what should be done in Mexico, San Francisco, Los Angeles—tremendous engineering undertakings to wipe out the danger in those areas. We need medical education and engineering education.

Dr. Banyai: Dr. Dean?

Dr. Dean: My opinion is that we must, first of all, ascertain the facts, just as we've been doing here and also from the various papers that have been published. Then we must use every reasonable means to bring the facts home to the public and to the medical profession. The medical schools, for instance, can be oriented to understand that air pollution is the modern equivalent of sewage pollution of 150 years ago, and something must be done about it. And, of course, the press should be utilized. We must help bring the matter home to industry. It's a matter of good public relations—the public don't like being poisoned and they don't like developing chronic bronchitis and lung cancer. If the industrialists want to keep on good terms with the public they must do something.

Dr. Banyai: Really well spoken.

Dr. Eastcott: I think that something has been done already as a result of various conferences held in California. I believe they have some legislation for controlling the exhausts of automobiles. I have noticed over the last 10 years that there have been considerable changes in England. Their smokeless stoves, though not very well abated at the moment, show steps in the right direction. I think that the public and people concerned with Public Health are at the moment very alive to this problem. So now is the time to keep pressing the evidence in support of the fact that atmospheric pollution is a bad thing.

Dr. Banyai: Thank you very much, Dr. Eastcott. Dr. Farber?

Dr. Farber: I think that, as members of the medical profession, we have an individual responsibility to patients to foster additional knowledge and support of research in the field of air pollution. It is through the efforts of the medical profession that the proper type of information can be given to the public.

I should like to point out, too, that we have not sufficiently utilized our potential resources for research. There have been studies on animals in cities as contrasted to the rural areas, for instance the increase of cancer in dogs living in cities as conrasted to the country. In cats, the increase in carcinoma of the tonsil, of the esophagus and stomach may be related to the fact that they lick their fur, and, perhaps, take in the carcinogens in this manner. There was a letter to the editor of the J.A.M.A., written by the distinguished Chauncey Leake, in which he describes conversations with Russian scientists. They, too, have noticed—just as in Holland and England—an increase in cancer in animals living in cities. So here we have throughout the world a group of trained scientists, the veterinarians, with whom the medical profession can combine in a specific effort to gain more information. I would like to list this as a research problem that should be considered.

Dr. Banyai: Dr. Flipse?

Dr. Flipse: It is a peculiarity of the human mind that those things we have had with us for a long time create less interest than matters which are of more recent development. Thus, the pollution of the atmosphere by radioactive materials, cancer in some scientists exposed to radiation and the concern about disposal of atomic wastes have produced a great deal of publicity. This has reached into the lives of the public because newspapers publish these things, so that now we find that many people do not like to have X-rays made. Exposure to radiant energy has been brought to their attention as a hazard. Meanwhile, they will continue to burn leaves and light bonfires to burn trash because atmospheric pollution has not come to their attention.

Pittsburgh, at one time, enjoyed a reputation as one of the smokiest cities in existence, but because of smoke abatement measures and ordinances and civic pride they have done tremendously well. So publicity is, after all, our greatest weapon.

Dr. Banyai: Thank you, Dr. Flipse. Dr. Ibrahim?

Dr. Ibrahim: In my opinion, all the known facts about air pollution, as discussed here, should be compiled in the form of a booklet or paper and disseminated among the medical profession. An organization should be started so that we can keep informed of results for mutual interest. More knowledge is needed concerning specific air pollutants in regard to the different factors which we have discussed. In my opinion, work should be started in small rural environments to obtain base-line studies where air pollution has not yet affected the environment, in East Pakistan, for example.

Dr. Banyai: Thank you, Dr. Ibrahim. Dr. Kaida?

Dr. Kaida: My opinion is as follows: 10 years ago bacterial contamination was one of the most important problems. Now problems of air contamination and nutrition have become the most important problems. We must get statistically valid data. We must continue our research from many points of view, as we discussed today, e.g. cancer, emphysema, bronchitis and others.

Dr. Banyai: Thank you, Dr. Kaida. Dr. Mancuso?

NEED FOR INTERNATIONAL RESEARCH ON AIR POLLUTION

Dr. Mancuso: I have several recommendations for consideration. All of you have heard of the International Geophysical Year which has established an excellent pattern for international cooperation and research. I should like to suggest a similar pattern and approach for research in air pollution. Actually, international cooperation in the study of our physical environment is not new. The International Geophysical Year was set up to observe geophysical phenomena and to secure data from all parts of the world. A large number and variety of scientific disciplines pooled their efforts so that each contributed to the overall mosaic of observations.

A similar approach could be considered for air pollution. In the Geophysical Year,

stations and networks were established according to an integrated plan. In the field of air pollution, there could be a similar series of networks and stations for the collection of air pollutants, utilizing international standards and uniform methods of sampling, identification and analysis. This, together with meteorological and other geophysical findings, would establish world-wide, basic data and provide the means for comparison and evaluation which are not possible at present.

There are a variety of different approaches between countries and within countries, states and metropolitan areas, in the methods used to characterize and quantitate atmospheric pollutants. This limits the interpretation that can be made of the data from various countries and areas. We might view air pollutants as a component of the total geophysical complex and proceed to develop a coordinated plan to study their various relationships. Most essential is the development of an agreed-upon basic plan of operations and research, integrated and carried out by the collaborating countries for the study of air pollutants. There is an obvious need for this collaboration in the development of an international plan and national plans for the study of the relationship of air pollution to health.

It is especially necessary to establish a basic organization and agreed-upon procedures for epidemiological surveillance of acute disasters as well as for the continued observation of the subacute and chronic endemic areas of atmospheric pollution. Pre-planning by the various biological, physical and chemical sciences is essential to develop an agreed-upon series of observations and procedures, if we are to derive meaningful data. Invariably such plans are developed when an acute episode has occurred and invariably the plans do not contain all the necessary data or specific procedures, so that subsequent interpretation of health effects is markedly handicapped. From an organizational point of view, we should, therefore, consider the development of a medical counterpart of the International Geophysical Year.

Now I should like to make two other points: one, there is another area that should be considered, and that is, the air as a mode of transmission of micro-organisms. It would seem desirable to explore more adequately the potentialities of the air as a means of transmission of microbiological organisms, harmful to plants and animals. Little is known of the actual microbiological population of the atmosphere and the concomitant effects of the aerial environment. It would seem that further research would be desirable and that, in conjunction with an international system of networks, microbiological air sampling should be carried out to determine the geographical distribution and identification of air-borne organisms, including fungi, bacteria, viruses and pollens, in addition to the identification and characterization of chemical air pollutants.

TISSUE CULTURE STUDIES OF AIR POLLUTANTS

Now, I have one final recommendation to make in relation to tissue culture on an international basis. I should like to recommend that an international committee on tissue culture and its relation to air pollution be established. This would have as its purpose the planning of studies on tissue culture as a sensitive toxicological approach to the investigation of air pollutants. In most of the toxicological work done it has been extremely difficult to produce or to ascertain acute effects on animals. But tissue culture methods, which actually have not been adequately explored, have been very successful in other areas. Procedures might be developed so that tissue culture might be able to telescope in time a whole series of experiments.

We have at the present time, in the tissue culture field, several cells—human skin, monkey skin, mouse fibroblast—that have been established and which can grow in entirely protein-free, chemically defined and antibiotic-free stable solutions. At the present time work is being done on tissue culture of human lung. It is worthwhile, in my opinion, to stimulate and encourage the development of a committee which would conduct a coordinated international plan of research so that each area may be working on a part of the mosaic. All together would provide results which may be meaningful.

Dr. Banyai: Thank you very much, Dr. Mancuso. Dr. Ono?

EDUCATION OF THE PUBLIC ON AIR POLLUTION

Dr. Ono: In educating the public on air pollution we have to incorporate the facts of the past. You all know what happened in the industrial Meuse Valley in Belgium, and at Donora, Pennsylvania. In 1952 about 4,000 London people died from smog. Now, these facts are not well known to the public. I think that public education must be imple-

mented with all these facts and many others. We have to have an international society for the prevention of air pollution. There was one meeting held last year in London called *Clean Air Conference*. We have to have national organizations, too. Last December in Japan the *National Society for the Prevention of Air Pollution* was organized.

Dr. Banyai: Thank you very much, Dr. Ono. Dr. Sirtori?

Dr. Sirtori: For the public, I think it is necessary to know that in animals living in zoos the lung cancer rate is increased, I think as a result of air pollution. And finally, it is necessary to discover an effective filter for automobile exhaust pipes.

Dr. Banyai: Thank you very much. Dr. Vorwald?

WHY WE NEED RESEARCH

Dr. Vorwald: Mr. Chairman, I would like to emphasize a few things. First, I place major emphasis on research. We must know, really, what atmospheric pollutants are present in the atmosphere and where they emanate from. Also, we need greater emphasis on the biochemical and physiological changes imposed on the biological system by atmospheric pollutants. I am somewhat tired of looking only at anatomical or structural changes and not knowing what goes on biochemically. In this, I think it important to consider tissue culture to at least give us some index as to the relative importance of one or the other atmospheric pollutants acting alone or in combination. While certainly of value for acute changes, I am somewhat dubious, however, whether tissue culture will tell us a great deal about chronic changes because of the limitations attendant on tissue culture.

Now, I think we have to do research in many areas, because if we don't, it becomes impossibles for us to teach and train medical students as to what biological effects certain pollutants have and what to look for. Teaching and training of medical students is important. We must train them to understand that the air around us is, indeed, not only oxygen and nitrogen, but that it contains a host of substances, all of which may play a role in the etiology of disease.

We mentioned here today chronic bronchitis and emphysema. From my point of view these are most serious problems today. We need epidemiological studies and biostatistical studies from a clinical point of view, which are very important and should be very carefully done. I question epidemiological studies which are based on death certificates because they deal with events which we cannot understand. We cannot go back, often 40 years, to identify in a death certificate what a man was exposed to. I cite in that regard some of our experimental evidence with respect to beryllium in cancer of the lung in albino rats. We exposed albino rats for 3 months and then had them live in clean air, and the frequency of cancer of the lung was comparable to that occurring in albino rats that had been exposed daily for 13 months. So it would seem, then, that with reference to identifying an etiological agent in the causation of a pulmonary disease, be it cancer or emphysema, we may have to go back many years to identify the challenge which may have occurred in the early lifetime of an individual and has not occurred since.

Research is most important. We must get on with knowing what our atmosphere contains. We are greatly concerned with ultramicroscopic particles which we haven't yet dealt with. We have dealt heretofore only with particles which we could see microscopically, larger than 0.2 microns in diameter; but today we are greatly interested in particles in the ultramicroscopic range, 0.002 microns, and what these do with respect to emphysema, changes in the bronchioles and in the alveolar septum. Then, we have to teach at the undergraduate and postgraduate level to inform the student, the medical man and the industrial hygienist as to the problems related to unclean air. Finally, with the knowledge gained from research, we can begin to educate the public.

I agree with Dr. Mancuso that we need an international group, because air pollution is now an international problem and nuclear energy has made it such. No longer is it a problem which is isolated. It is worldwide and I would like to know precisely what the atmospheric pollution problems are in Iceland, in India, in Japan, in China. If we could know them we might be able to relate the incidence of disease to certain pollutants. So, from research and from the knowledge derived from research we will know what to teach our medical students and we will have the knowledge to tell the people what to do about atmospheric pollution.

Dr. Banyai: Thank you, Dr. Vorwald. Before closing this intellectually stimulating and scientifically profitable conference, I want to thank every one of you for your splendid contributions.

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Professor and Director, National Institute for the Study and Treatment of Tumors, Division of Anatomy and Pathological Histology, Milan, Italy.
13. Arthur J. Vorwald, M.D.
Professor and Chairman, Department of Industrial Medicine and Hygiene, Wayne State University, Detroit, Michigan, U.S.A.

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mented with all these facts and many others. We have to have an international society for the prevention of air pollution. There was one meeting held last year in London called *Clean Air Conference*. We have to have national organizations, too. Last December in Japan the *National Society for the Prevention of Air Pollution* was organized.

Dr. Banyai: Thank you very much, Dr. Ono. Dr. Sirtori?

Dr. Sirtori: For the public, I think it is necessary to know that in animals living in zoos the lung cancer rate is increased, I think as a result of air pollution. And finally, it is necessary to discover an effective filter for automobile exhaust pipes.

Dr. Banyai: Thank you very much. Dr. Vorwald?

WHY WE NEED RESEARCH

Dr. Vorwald: Mr. Chairman, I would like to emphasize a few things. First, I place major emphasis on research. We must know, really, what atmospheric pollutants are present in the atmosphere and where they emanate from. Also, we need greater emphasis on the biochemical and physiological changes imposed on the biological system by atmospheric pollutants. I am somewhat tired of looking only at anatomical or structural changes and not knowing what goes on biochemically. In this, I think it important to consider tissue culture to at least give us some index as to the relative importance of one or the other atmospheric pollutants acting alone or in combination. While certainly of value for acute changes, I am somewhat dubious, however, whether tissue culture will tell us a great deal about chronic changes because of the limitations attendant on tissue culture.

Now, I think we have to do research in many areas, because if we don't, it becomes impossibles for us to teach and train medical students as to what biological effects certain pollutants have and what to look for. Teaching and training of medical students is important. We must train them to understand that the air around us is, indeed, not only oxygen and nitrogen, but that it contains a host of substances, all of which may play a role in the etiology of disease.

We mentioned here today chronic bronchitis and emphysema. From my point of view these are most serious problems today. We need epidemiological studies and biostatistical studies from a clinical point of view, which are very important and should be very carefully done. I question epidemiological studies which are based on death certificates because they deal with events which we cannot understand. We cannot go back, often 40 years, to identify in a death certificate what a man was exposed to. I cite in that regard some of our experimental evidence with respect to beryllium in cancer of the lung in albino rats. We exposed albino rats for 3 months and then had them live in clean air, and the frequency of cancer of the lung was comparable to that occurring in albino rats that had been exposed daily for 13 months. So it would seem, then, that with reference to identifying an etiological agent in the causation of a pulmonary disease, be it cancer or emphysema, we may have to go back many years to identify the challenge which may have occurred in the early lifetime of an individual and has not occurred since.

Research is most important. We must get on with knowing what our atmosphere contains. We are greatly concerned with ultramicroscopic particles which we haven't yet dealt with. We have dealt heretofore only with particles which we could see microscopically, larger than 0.2 microns in diameter; but today we are greatly interested in particles in the ultramicroscopic range, 0.002 microns, and what these do with respect to emphysema, changes in the bronchioles and in the alveolar septum. Then, we have to teach at the undergraduate and postgraduate level to inform the student, the medical man and the industrial hygienist as to the problems related to unclean air. Finally, with the knowledge gained from research, we can begin to educate the public.

I agree with Dr. Mancuso that we need an international group, because air pollution is now an international problem and nuclear energy has made it such. No longer is it a problem which is isolated. It is worldwide and I would like to know precisely what the atmospheric pollution problems are in Iceland, in India, in Japan, in China. If we could know them we might be able to relate the incidence of disease to certain pollutants. So, from research and from the knowledge derived from research we will know what to teach our medical students and we will have the knowledge to tell the people what to do about atmospheric pollution.

Dr. Banyai: Thank you, Dr. Vorwald. Before closing this intellectually stimulating and scientifically profitable conference, I want to thank every one of you for your splendid contributions.

PARTICIPANTS IN THE CONFERENCE

1. Donato G. Alarcon, M.D.
Medical Director, Sanatorio San Angel; Professor of Clinical Medicine, National University, Mexico City, Mexico.
2. Andrew L. Banyai, M.D.
Clinical Professor of Medicine, Emeritus, Marquette University School of Medicine (Milwaukee, Wisconsin), Chicago, Illinois, U.S.A.
3. Geoffrey Dean, M.D., M.R.C.P. (Lond.)
Senior Physician, Eastern Cape Provincial Hospital, Port Elizabeth, South Africa.
4. David F. Eastcott, M.D., B.S., D.P.H.
Formerly Assistant Director, National Health Institute, New Zealand.
5. Seymour M. Farber, M.D.
Chief, University of California Tuberculosis and Chest Service, San Francisco General Hospital; Assistant Dean—Continuing Education in Medicine and the Health Sciences, University of California Medical Center, San Francisco, California, U.S.A.
6. M. Jay Flipse, M.D.
Practitioner of Internal Medicine; President, American College of Chest Physicians; Chief Consultant, Service of Pulmonary Diseases, Jackson Memorial Hospital; Chief of the Service of Medicine, Dade County Hospital; Associate Clinical Professor of Medicine, University of Miami School of Medicine, Miami, Florida, U.S.A.
7. Mohammed Ibrahim, M.B., M.R.C.P. (Lond.)
Professor of Clinical Medicine, Medical College Hospital, Dacca, East Pakistan.
8. Katsumi Kaida, M.D.
Director, Research Institute for Diseases of the Chest; Professor, Faculty of Medicine, Kyushu University, Fukuoka, Japan.
9. Thomas F. Mancuso, M.D.
Chief, Division of Industrial Hygiene, Ohio Department of Health, Columbus, Ohio, U.S.A.
10. Jo Ono, M.D.
Visiting Professor of Bronchoesophagology, Keio University School of Medicine, Tokyo, Japan.
11. Bernard Pierson, M.D.
Pathologist; Chief of Research, Cancer Institute, University of Nancy, France.
12. Carlo Sirtori, M.D.
Professor and Director, National Institute for the Study and Treatment of Tumors, Division of Anatomy and Pathological Histology, Milan, Italy.
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NEOSPORIN ANTIBIOTIC OINTMENT

Burroughs Wellcome & Co. (South Africa) Ltd. announce the introduction of **Neosporin** Antibiotic Ointment for topical and ophthalmic use.

This preparation of 3 antibiotics, incorporated in a stable petroleum base for topical use, contains 5,000 units of **Aerosporin** brand *Polymyxin B* Sulphate; 400 units Zinc *Bacitracin;* and 5 mg. *Neomycin Sulphate* in each gramme. This combination provides bactericidal action against virtually the whole range of bacteria likely to appear topically. Thus, it acts not only against primary pathogens, but as a guard against secondary invaders.

Aerosporin has a bactericidal action against most Gram-negative bacilli and is particularly effective against *Ps. pyocyanea* (*Ps. aeruginosa*). Pseudomonas organisms readily gain access to the skin and to lesions from air and occasionally from instruments, dressings and drug solutions. Bacitracin is active against Gram-positive organisms as well as gonococci and *Treponema pallidum*. Bacitracin is not inhibited by those organisms which produce penicillinase. Neomycin Sulphate is particularly effective against Proteus organisms which commonly contaminate skin lesions and which are highly resistant to other agents. The antibiotics diffuse readily from the ointment base into the fluids of the skin and tissues and promote more rapid healing than with cream or water-miscible bases. The non-aqueous base ensures stability of all the antibiotics and **Neosporin** will retain its potency for about three years at room temperature.

The use of **Neosporin** for local lesions avoids possible sensitization to penicillin, streptomycin and the broad-spectrum antibiotics. Development by bacteria of resistance to **Neosporin** has rarely been shown during clinical application. All 3 antibiotics have very low indices of allergenicity; used locally, **Neosporin** is non-irritating, there is no significant systemic absorption of the antibiotics and side-effects are not to be expected. The extreme rarity of either sensitization or bacterial resistance allows **Neosporin** to be used for long periods or repeatedly if required.

Indications: **Neosporin** may be used in the treatment of infected wounds, burns or skin grafts, and it is also of value in the preparation of donor sites for skin grafting and in the prevention of infection of extensive burns and contaminated wounds. It is of value in the local treatment of chronic varicose or other indolent ulcers, for which purpose it may be used in conjunction with **Dornokinase** brand Streptokinase-Streptodornase.

The preparation is also of value in the treatment of furuncles, carbuncles, pyoderma, sycosis barbae, impetigo and acne. It has also been used in dealing with secondarily infected skin lesions of scabies, pediculosis, tinea pedis and contact and allergic dermatitis. Ocular infections due to susceptible organisms respond well to **Neosporin.** Being bland and non-irritating, its application to the sensitive structures of the eye is well tolerated. Conditions which have responded favourably to treatment with the ointment include styes, conjunctivitis, scleritis, keratitis, corneal ulcers and blepharitis. It may also be used prophylactically after the removal of foreign bodies from the eye and in pre-operative management.

Presentation: Collapsible tubes of 2 and 5 g. (with special nozzle for ophthalmic use).

Price to Public: 2 g.: R 0.30. 5 g.: R 0.65.

Further information may be obtained from:

Burroughs Wellcome & Co. (South Africa) Ltd., P.O. Box 10293, Johannesburg.

MUCAINE

FOR GASTRITIS AND RELATED DISORDERS

A new and original Wyeth development now offers a unique product for the treatment of gastritis and related disorders. **Mucaine** contains the first practical mucosal anaesthetic, Oxethazaine, in a base of alumina gel and magnesium hydroxide. Oxethazaine is the result of Wyeth's extensive research and clinical trials over a 5-year period.

Mucaine is an antacid, demulcent and mucosal anaesthetic in the form of a truly palatable liquid. Each 5 c.c. teaspoonful contains 10 mg. of Oxethazaine in aluminium hydroxide and magnesium hydroxide gel. Oxethazaine is a very active topical anaesthetic which is 4,000 times more potent than Procaine. Furthermore, Oxethazaine provides anaesthesia of much longer duration. Despite this potency, however, it has a wide margin of safety as supplied in this compound. Therapeutic doses have not produced toxicity even after continued administration.

Mucaine is indicated for many gastric disorders which are not totally managed by diet, antacids and anticholinergics. It provides prolonged anaesthesia of oesophageal and gastric mucosa despite the ebb and flow of gastric contents. As reported by Deutsch and Christian in J.A.M.A. **169**:2012 (25 April) 1959, **Mucaine** brought complete relief to 96% of 92 patients who suffered substernal pain and upper abdominal distress. The remaining 4% received partial relief.

Mucaine, therefore, offers an effective new way to treat such symptoms of gastritis, oesophagitis and irritable bowel as indigestion, heartburn, dyspepsia, nausea, vomiting and bloating. **Mucaine** aids recovery through its multiple action. Most significantly, it enables patients to accept food in greater volume and variety because of the relief from pain afforded by the anaesthetic action.

Dosage: **Mucaine** has a simple dosage regimen: one or two teaspoonsful 4 times daily, 15 minutes before meals and at bedtime. This regimen is facilitated by the fact that **Mucaine** is palatable, even over long-term administration. Certain precautions should be observed. Some patients may experience dizziness, faintness or drowsiness if the daily dosage of **Mucaine** exceeds 12 teaspoonsful. However, Deutsch and Christian reported that 'no significant side-effects developed' among their patients.

Package Size: Bottles of 6 fl. oz.

Mucaine represents a significant advance in the treatment of a major medical field, gastritis. **Mucaine** is unique. Because of its potent but safe topical anaesthetic action together with its antacid and demulcent qualities, **Mucaine** accomplishes what no other drug on the market to-day can do.